REMARKS

Applicant's attorney wishes to thank the Examiner for her cooperation in response to a telephone discussion regarding this application. In accordance with the Examiner's suggestion, the following amendment is submitted. However, applicant's attorney is ready to discuss the application following review of the amendment by the Examiner.

Claim 1 has been amended, claim 22 has been cancelled without prejudice, and claims 1-21 and 23-26 are presently pending in the application.

The Examiner objected to the drawings regarding a failure to show the subject matter of amended claim 22. Since that claim has now been cancelled without prejudice, this objection is not moot.

In a similar fashion, the claim 22 renders moot the rejection under 35 U.S.C., first paragraph, set forth in paragraph 4 of the Office Action.

The Examiner also rejected claims 1-26 under U.S.C. §112 ¶2. In this regard, the Examiner rejected previous claim 1 with respect to the language "a large-area rectangular field of a microplate." In particular, the Examiner stated that the term "large" is a relative term and is therefore unclear. As now set forth in claim 1 as amended, the "large-area rectangular field" is defined by the linear dimension of said at least one linear dispensing cone due to said number of nozzles over the comb in relation to the well pitch in one dimension of the microplate and, in the other dimension, by a plurality of microplate columns being progressively dispensed due to the displacement of the at least one linear dispensing comb." Accordingly, the objection to the use of the term "large" has been clarified by this additional language and the rejection is therefore fully traversed.

The Examiner further states with regard to clarity concerning claim 1 that the language previously set forth regarding the imaging camera is functional, which renders the claim indefinite. As now set forth, the "imaging camera" is "for receiving an image of said large-area rectangular field provided by said imaging optical system, the imaging camera and said imaging optical system provided in a camera block being directed to the underside of the microplate across from the dispensing unit, the imaging camera being a video camera for repeatedly receiving and storing a plurality of images over time, each image including all wells of the large-area rectangular field of the microplate, so that a course of luminescence over time for each individual specimen in all wells of the large-area rectangular field is measurable while

simultaneously ongoing dispensing occurs successively column by column." With this additional defining language, it is believed that the indefiniteness suggested by the Examiner has been fully traversed.

Also, the "imaging optical system" has been clarified by the language referred to previously concerning the "large-area rectangular field." Thus, based on the above, a person of ordinary skill in the art would clearly know that the imaging optical system is responsible for creating an image and that the imaging camera is intended for receiving the optical image and converting it into electronic data storing and further processing and "repeatedly receiving an image." It is done by regularly or continual readouts of the camera and storing of progressively derived electronic image data.

The Examiner also rejected claim 22 under 35 U.S.C. §112 ¶2; however, as explained above, that claim has been cancelled, and therefore this rejection is rendered moot.

The Examiner has also rejected claims 1-5, 8, 9, 11, 20 and 23-26 under 35 U.S.C. §103(a) as being unpatentable over Geibeler et al. With the amendment of claim 1, it is believed that applicant's invention has been more particularly pointed out and distinguishes clearly over Giebeler. Similarly, the combinations of Giebeler in view of Wohlstadter et al. and Marouiss et al. and Schick under 35 U.S.C. §103(a) has been overcome by the revision of claim 1. The following additional discussion is presented to highlight the patentable distinctions of applicant's claimed invention.

In order to further point out distinctions over Giebeler, reference is made to the optical and detector system of Giebeler and many of the mischaracterizations and misunderstandings of the Examiner stated in the outstanding Office Action in this regard.

According to the present invention, and in total contrast to Giebeler, the progressively dispensed and permanently imaged large-area rectangular field of the microplate compares to an observation of the night sky in awaiting shooting stars.

Firstly, the light intensities of both observation tasks are similar because the fluorescent light is very weak as well as the flow of shooting stars. Secondly, a fluorescence reaction often occurs only in a few wells, the position of which is not known before. Thirdly, the peak fluorescence in the dispensed wells can differ from one to another in brightness and in time scale nearly accidentally similar to shooting star occurrence in August (i.e., you know that it occurs regularly; however, you do not k now when and how intensive it happens).

In contrast to all Giebeler approaches, the fluorescence measurement according to the invention is derived from the light spots of all imaged wells of the observed rectangular field regardless of the time dependence of the samples' individual response characteristics and of the scheme of dispensing. The dispensing scheme is only used for evaluation, if necessary, of the delay time of the fluorescence peak from the time when dispensing into a specific well, wherein the determination of delay time is performed after the complete measurement (i.e., repeated imaging and storing) has been done.

The knowledge and the value of fluorescence delay time is not needed, either for the correct measurement of the course of fluorescence or for the controlling "...'repeatedly receiving an image' can be coordinated with the process of measuring the 'course of luminescence over time'..." referred to in the Office Action. The reason is that the dispensing is timely constant progressing and accordingly the fluorescence is progressively occurring; however, if it differs in expected delay time, it can be evaluated afterwards.

The measurement is done independently from column-to-column dispensing velocity by permanently imaging and storing the intensity data of the whole observed rectangular field over time (dispensing time plus expected response time for the latest dispensed column of the observed rectangular field).

In comparison to Giebeler, the fluorescence measurements according to the invention are received much faster, time-resolved and independent from the dispensing scheme and velocity; i.e., the dispensing velocity is neither limited by a delay-time for transportation of the dispensed well column to a measurement module nor by the measurement time itself; double-dispensing does not require a further measurement procedure but is derived from the same measurement (permanent rectangular field observation).

The above-mentioned features and advantages represent the kernel teaching of the invention and is neither anticipated by nor obviously derivable from Giebeler who only discloses a single well detection without optically imaging the microplate (or a substantial part of it).

While Giebeler disclosed "top and bottom optics," applicant wants to point out that the top and bottom optics are only mentioned for "enabling a variety of measurement modes" within the analysis module that is separated from the dispenser module and only connected to it by a transport module. "...including...bottom illumination and bottom detection..." was not disclosed as being in any relationship to the dispenser module and is never to be understood as a

suggestion to be arranged across to the dispenser. While Giebeler mentioned a photodiode array or a suitable CCD, the Examiner is clearly incorrect in asserting that the "suitable CCD, rectangular or square" as mentioned by Giebeler could be understood as an "imaging camera" because the CCD is only used as an array of single detector elements that are coupled to the microplate wells exclusively by a plurality of fiber transmission optics. There is no imaging taught and also no measurement simultaneous to the dispensing. All the optics shown in the figures are intended to collect the divergent fluorescent light before coupling into the fiber for guiding to one defined CCD element. That has nothing to do with imaging.

As paragraph [0092] is concerned, the bottom detection of light is only shown as an alternative measurement position to enable reflective and transmissive detection of light under illumination from top to bottom.

Referring to paragraphs [0246] and [0247], Giebeler only discloses dispensing a higher number of wells (or even all wells) of the microplate within a fluidics module, then moving these wells by a transport module to an analysis module to detect the amount of luminescence light that is emitted after a defined delay time. There is no hint that any other scheme than that of paragraph [0030] shall be used. The only teaching of paragraph [0247] is to dispense more wells at once and to detect more wells at once; i.e., a higher number of wells simultaneous, but both steps separated (because of the desired time-delayed measurement, after transportation).

Also with respect to the transparent bottoms of the microplate wells, there is no teaching of measuring simultaneous to the dispensing but only a disclosure of one embodiment for the measurement within the separated analysis module Giebeler has neither shown nor described to perform the measurement simultaneous to the dispensing.

Even if Giebeler disclosed to simultaneously detect a plurality of wells or even all wells, it is only derived from paragraph [0247] to extend the analysis module in the following way:

- light is provided from a lamp via a monochromator and then divided and distributed by a number of **n** light guiding fibers to **n** wells of the microplate;
- the response light of the substance(s) in the **n** wells is coupled into **n** separate reading heads, which are consisting of **n** (mirror) optics (derived from Fig. 10) and into **n** light guiding fibers;
- the light guided by the **n** fibers and coupled out of the **n** fibers are focused onto **n** detectors that are not necessarily single ones but can also be separate detector elements of

a 2D detector array (suitable CCD). (See Fig. 10 for one well only, and [0246, 0247] for extension to a multiplicity of wells.)

Consequently, there is no teaching of Giebeler:

1. neither to use an objective for imaging a large-area rectangular field of the microplate onto an image sensor, but only to bundle the light of each single well and to transmit it to one single detector element associated by an optical fiber; nor

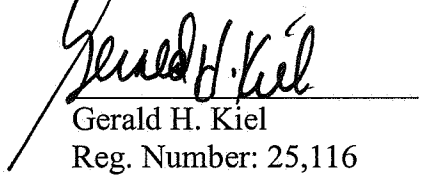
2. to have a combined fluidics and analysis module, which would supersede the transportation module; i.e., make it unnecessary (paragraph [0247] never teaches to simultaneously combine simultaneous dispensing with simultaneous detection of multiple wells).

Insofar as the Examiner asserts that Giebeler did "not specifically disclose the relative size of the 'area'" of the plurality of wells, applicant disagrees with this statement because of the mixing of different facts.

While Giebeler disclosed raising throughput of the device by simultaneously dispensing more than one row of wells and to (separately, time-delayed) observe more than one row of wells, Giebeler does not disclose an imaging of an area of wells, but only single-well light detection. There is no optical image of an area of wells. The CCD is only used by Giebeler as an array of single detectors, each of which is separately connected to one associated well. All optics shown by Giebeler are light-collecting optics for a single well only. Thus, there is no disclosure or suggestion of imaging a whole area of the microplate by an optical imaging system.

Applicant submits that the patentable distinctions from Giebeler have been more particularly pointed out and distinguished in amended claim 1, taken together with the extensive discussion of the technology presented above. It is submitted therefore that all of the claims presently in the application should now be allowed, and that the application should be passed to issue at the earliest opportunity. If this amendment does not enter for purposes of allowance, please enter it for purposes of appeal.

Respectfully submitted,



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